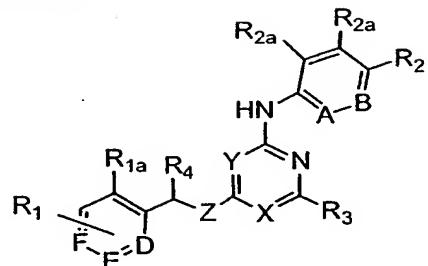


What is claimed is:

1. A compound of the formula:



or a pharmaceutically acceptable form thereof, wherein:

A and B are independently CR_{2a} or N;

D, E and F are independently CH or N;

X and Y are independently CR_x or N;

R_x is independently chosen at each occurrence from hydrogen, C₁-C₆alkyl, amino, and mono- and di-(C₁-C₆alkyl)amino;

Z is O or NR_z; wherein R_z is hydrogen, C₁-C₆alkyl or taken together with R_{1a} to form a fused heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C₁-C₆alkyl, C₁-C₆alkoxy and C₁-C₆haloalkyl;

R_{1a} is:

(i) chosen from halogen, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;

(ii) taken together with R_z to form a fused heterocyclic ring; or

(iii) taken together with R₄ to form a fused carbocyclic ring;

R₁ represents from 0 to 2 substituents independently chosen from halogen, hydroxy, amino, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;

R₂ and each R_{2a} are independently chosen from hydrogen, hydroxy, amino, halogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;

R₃ is selected from:

- (i) halogen, hydroxy and haloC₁-C₆alkyl;
- (ii) phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and
- (iii) groups of the formula:



wherein

L is a single covalent bond or C₁-C₆alkylene;

R₅ and R₆ are:

- (a) independently chosen from hydrogen, C₁-C₈alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 7-membered heterocycloalkyl)C₀-C₄alkyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl, such that if L is a single bond, then R₅ and R₆ are not phenyl or pyridyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and

R₄ is hydrogen, C₁-C₆alkyl or taken together with R_{1a} to form a fused carbocyclic ring.

2. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein R₁ represents 0 substituents.

3. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein R_{1a} is halogen, cyano, -COOH, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkylsulfonyl, or mono- or di-(C₁-C₆alkyl)sulfonamido.

4. A compound or pharmaceutically acceptable form thereof according to claim 3, wherein R_{1a} is fluoro, chloro, cyano, methyl, trifluoromethyl or methylsulfonyl.

5. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein R₃ is selected from:

- (i) halogen, hydroxy and C₁-C₆haloalkyl;
- (ii) phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and

(iii) groups of the formula $-N(R_5)(R_6)$ and $-O-R_7$, wherein:

R_5 and R_6 are:

- (a) independently chosen from hydrogen, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_1-C_8 alkenyl, C_2-C_8 alkanoyl, benzyl and $-CH_2$ -pyridyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R_7 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_1-C_8 alkenyl or C_2-C_8 alkanoyl;

wherein each of (ii) and (iii) is substituted on from 0 to 3 carbon atoms with substituents independently chosen from halogen, cyano, amino, hydroxy, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_2-C_6 alkyl ether, C_1-C_6 alkoxy, C_2-C_6 alkanoyl, C_1-C_6 haloalkyl, mono- and di-(C_1-C_6 alkyl)amino and 4- to 8-membered heterocycloalkyl; and

6. A compound or pharmaceutically acceptable form thereof according to claim 5, wherein R_3 is a group of the formula $-N(R_5)(R_6)$, wherein R_5 and R_6 are:

- (a) independently chosen from hydrogen, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_1-C_6 alkenyl, benzyl and $-CH_2$ -pyridyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

wherein each of which alkyl, cycloalkyl, alkenyl, benzyl, pyridyl and heterocycloalkyl is substituted with from 0 to 3 substituents independently chosen from halogen, amino, cyano, hydroxy, C_1-C_4 alkyl, C_2-C_4 alkyl ether, C_1-C_4 alkoxy, C_1-C_4 haloalkyl and mono- and di-(C_1-C_4 alkyl)amino.

7. A compound or pharmaceutically acceptable form thereof according to claim 6, wherein R_3 is mono- or di-(C_1-C_6 alkyl)amino.

8. A compound or pharmaceutically acceptable form thereof according to claim 6, wherein R_3 is benzylamino or $-NH-CH_2$ -pyridyl, each of which is substituted with from 0 to 2 substituents independently chosen from halogen, amino, hydroxy, cyano, C_1-C_4 alkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl.

9. A compound or pharmaceutically acceptable form thereof according to claim 6, wherein R_3 is pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl or azepanyl, each of which is substituted with from 0 to 3 substituents independently chosen from halogen, amino, hydroxy, cyano, C_1-C_4 alkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl.

10. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein R_3 is a group of the formula $-O-R_7$ wherein R_7 is hydrogen, C_1-C_6 alkyl, phenyl C_0-

C₆alkyl or pyridylC₀-C₆alkyl, wherein each alkyl, phenyl and pyridyl is substituted with from 0 to 3 substituents independently chosen from halogen, hydroxy, cyano, amino, C₁-C₄alkyl, C₁-C₄haloalkyl and C₁-C₄alkoxy.

11. A compound or pharmaceutically acceptable form thereof according to claim 10, wherein R₃ is benzyloxy or -O-CH₂-pyridyl, each of which is substituted with from 0 to 2 substituents independently chosen from halogen, hydroxy, cyano, amino, C₁-C₄alkyl, C₁-C₄haloalkyl and C₁-C₄alkoxy.

12. A compound or pharmaceutically acceptable form thereof according to claim 10, wherein R₃ is C₁-C₆alkoxy.

13. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein R₂ and each R_{2a} are independently chosen from hydrogen, amino, halogen, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkylsulfonyl and mono- and di-(C₁-C₄alkyl)sulfonamido, and wherein at least one of R₂ or R_{2a} is not hydrogen.

14. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein R₂ is halogen, C₁-C₆alkyl or C₁-C₄haloalkyl.

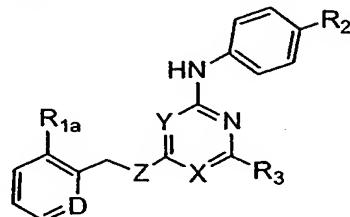
15. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein X is N.

16. A compound or pharmaceutically acceptable form thereof according to claim 15, wherein Y is N.

17. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein Z is O.

18. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein Z is NH.

19. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein the compound has the formula:



20. A compound or pharmaceutically acceptable form thereof according to claim 19, wherein:

R_{1a} is fluoro, chloro, cyano, methyl, trifluoromethyl or methylsulfonyl;

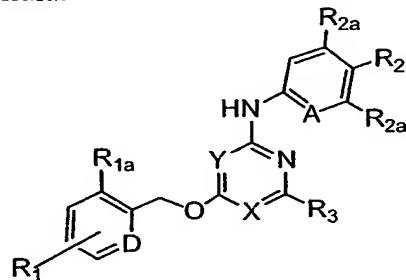
R₂ is halogen, C₁-C₄alkyl or C₁-C₄haloalkyl;

R₃ is: (i) halogen, hydroxy or amino; or

(ii) mono- or di-(C₁-C₆alkyl)amino, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl, benzyloxy or -N-CH₂-pyridyl, each of which is substituted with from 0 to 2 substituents independently chosen from halogen, amino, hydroxy, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₄haloalkyl and mono- and di-(C₁-C₆alkyl)amino; and

Z is O or NH.

21. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein the compound has the formula:



22. A compound or pharmaceutically acceptable form thereof according to claim 21, wherein A is N or CH and at least one R_{2a} or R₂ is not hydrogen.

23. A compound or pharmaceutically acceptable form thereof according to claim 22, wherein:

R_{1a} is fluoro, chloro, cyano, methyl, trifluoromethyl or methylsulfonyl;

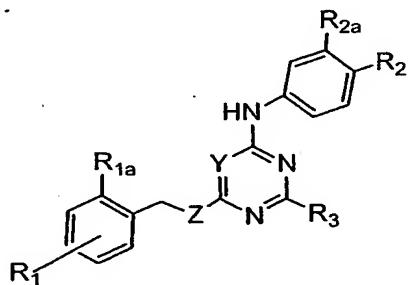
R₁ represents zero or one substituent;

R₂ and each R_{2a} are independently chosen from hydrogen, halogen, C₁-C₄alkyl, and C₁-C₄haloalkyl, such that at least one R_{2a} or R₂ is not hydrogen; and

R₃ is: (i) halogen, hydroxy or amino; or

(ii) mono- or di-(C₁-C₆alkyl)amino, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl, benzyloxy or -N-CH₂-pyridyl, each of which is substituted with from 0 to 2 substituents independently chosen from halogen, amino, hydroxy, C₁-C₄alkyl, cyano, C₁-C₄alkoxy, C₁-C₄haloalkyl and mono- and di-(C₁-C₆alkyl)amino.

24. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein the compound has the formula:



25. A compound or pharmaceutically acceptable form thereof according to claim 24, wherein at least one of R₂ and R_{2a} is not hydrogen.

26. A compound or pharmaceutically acceptable form thereof according to claim 25, wherein:

R_{1a} is fluoro, chloro, cyano, methyl or trifluoromethyl;

R₁ represents zero one or substituent;

R₂ and R_{2a} are independently chosen from hydrogen, halogen, C₁-C₄alkyl, and C₁-C₄haloalkyl;

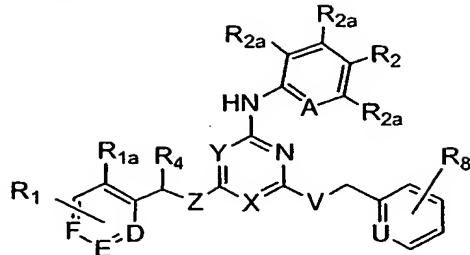
R₃ is: (i) halogen, hydroxy or amino; or

(ii) mono- or di-(C₁-C₆alkyl)amino, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl, benzyloxy or -N-CH₂-pyridyl, each of which is substituted with from 0 to 2 substituents independently chosen from halogen, amino, hydroxy, C₁-C₄alkyl, cyano, C₁-C₄alkoxy, C₁-C₄haloalkyl and mono- and di-(C₁-C₆alkyl)amino; and

Z is O or NH.

27. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein the compound exhibits no detectable agonist activity an *in vitro* assay of capsaicin receptor agonism.

28. A compound of the formula:



or a pharmaceutically acceptable form thereof, wherein:

A is CR_{2a} or N;

D, E, F and U are independently CH or N;

X and Y are independently CR_x or N;

R_x is independently chosen at each occurrence from hydrogen, C₁-C₆alkyl, amino, cyano, and mono- and di-(C₁-C₆alkyl)amino;

Z is O or NR_z; wherein R_z is hydrogen, C₁-C₆alkyl or taken together with R_{1a} to form a fused heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C₁-C₆alkyl, C₁-C₆alkoxy and C₁-C₆haloalkyl;

V is O or NR_v; wherein R_v is hydrogen, C₁-C₆alkyl or taken together with an R₈ to form a fused heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C₁-C₆alkyl, C₁-C₆alkoxy and C₁-C₆haloalkyl;

R_{1a} is:

- (i) chosen from halogen, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or
- (ii) taken together with R₂ to form a fused heterocyclic ring; or
- (iii) taken together with R₄ to form a fused carbocyclic ring;

R₁ represents from 0 to 2 substituents independently chosen from halogen, hydroxy, amino, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;

R₈ represents from 0 to 3 substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or R₈ is taken together with R_v to form a fused heterocyclic ring;

R₂ and each R_{2a} are independently chosen from hydrogen, hydroxy, amino, cyano, halogen, C₁-C₆alkyl, C₁-C₆haloalkyl, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and

di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; and

R₄ is hydrogen, C₁-C₆alkyl or taken together with R_{1a} to form a fused carbocyclic ring.

29. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein R₁ represents 0 substituents.

30. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein R_{1a} is halogen, cyano, -COOH, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkylsulfonyl, or mono- and di-(C₁-C₆alkyl)sulfonamido.

31. A compound or pharmaceutically acceptable form thereof according to claim 30, wherein R_{1a} is fluoro, chloro, cyano, methyl, trifluoromethyl or methylsulfonyl.

32. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein each R_{2a} and R₂ are independently chosen from hydrogen, amino, halogen, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkylsulfonyl and mono- and di-(C₁-C₄alkyl)sulfonamido, such that at least one of R_{2a} and R₂ is not hydrogen.

33. A compound or pharmaceutically acceptable form thereof according to claim 32, wherein R₂ is not hydrogen.

34. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein X is N.

35. A compound or pharmaceutically acceptable form thereof according to claim 34, wherein Y is N.

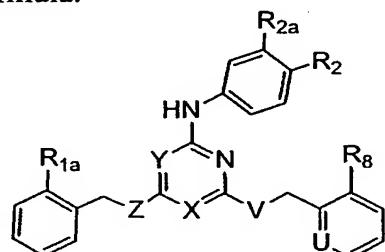
36. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein Z is O.

37. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein Z is NH.

38. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein V is O.

39. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein V is NH.

40. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein the compound has the formula:



wherein R₈ is halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, C₂-C₆alkyl ether, C₂-C₄alkanoyl, C₃-C₄alkanone, C₁-C₄haloalkyl, C₁-C₄haloalkoxy, mono- and di-(C₁-C₄alkyl)amino, C₁-C₄alkylsulfonyl, mono- or di-(C₁-C₄alkyl)sulfonamido, or mono- or di-(C₁-C₄alkyl)aminocarbonyl.

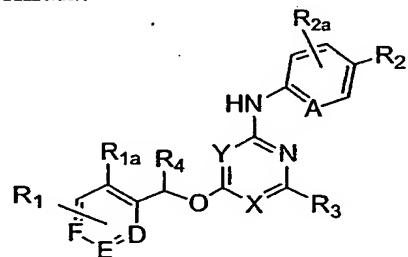
41. A compound or pharmaceutically acceptable form thereof according to claim 40, wherein:

R_{1a} and R₈ are independently fluoro, chloro, cyano, methyl, trifluoromethyl or methylsulfonyl;

R₂ and R_{2a} are independently chosen from hydrogen, halogen, C₁-C₄alkyl, and C₁-C₄haloalkyl, with the proviso that at least one of R₂ and R_{2a} is not hydrogen; and V and Z are independently NH or O.

42. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein the compound exhibits no detectable agonist activity an *in vitro* assay of capsaicin receptor agonism.

43. A compound of the formula:



or a pharmaceutically acceptable form thereof, wherein:

A, D, E and F are independently CH or N;

X and Y are independently CR_x or N;

R_x is independently chosen at each occurrence from hydrogen, C_1 - C_6 alkyl, amino, and mono- and di-(C_1 - C_6 alkyl)amino;

R_{1a} is:

- (i) chosen from halogen, cyano, amino, -COOH, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_1 - C_6 haloalkyl, C_1 - C_6 haloalkoxy, mono- and di-(C_1 - C_6 alkyl)amino, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)sulfonamido, and mono- and di-(C_1 - C_6 alkyl)aminocarbonyl; or
- (ii) taken together with R_4 to form a fused carbocyclic ring;

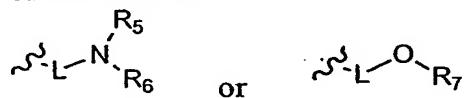
R_1 represents from 0 to 2 substituents independently chosen from halogen, hydroxy, amino, cyano, -COOH, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_2 - C_6 alkyl ether, C_2 - C_6 alkanoyl, C_3 - C_6 alkanone, C_1 - C_6 haloalkyl, C_1 - C_6 haloalkoxy, mono- and di-(C_1 - C_6 alkyl)amino, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)sulfonamido, and mono- and di-(C_1 - C_6 alkyl)aminocarbonyl;

R_2 is chosen from hydroxy, amino, cyano, halogen, hydroxy, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 alkoxy, C_2 - C_6 alkyl ether, C_2 - C_6 alkanoyl, C_3 - C_6 alkanone, mono- and di-(C_1 - C_6 alkyl)amino, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)sulfonamido, and mono- and di-(C_1 - C_6 alkyl)aminocarbonyl;

R_{2a} represents from 0 to 2 substituents independently chosen from hydroxy, amino, cyano, halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl, C_1 - C_6 alkoxy, C_2 - C_6 alkyl ether, C_2 - C_6 alkanoyl, C_3 - C_6 alkanone, mono- and di-(C_1 - C_6 alkyl)amino, C_1 - C_6 alkylsulfonyl, mono- and di-(C_1 - C_6 alkyl)sulfonamido, and mono- and di-(C_1 - C_6 alkyl)aminocarbonyl;

R_3 is selected from:

- (i) halogen, hydroxy and halo C_1 - C_6 alkyl;
- (ii) phenyl C_0 - C_4 alkyl and pyridyl C_0 - C_4 alkyl; and
- (iii) groups of the formula:



wherein

L is a single covalent bond or C_1 - C_6 alkylene;

R_5 and R_6 are:

- (a) independently chosen from hydrogen, C_1 - C_8 alkyl, C_1 - C_8 alkenyl, C_2 - C_8 alkanoyl, (C_3 - C_8 cycloalkyl) C_0 - C_4 alkyl, (3- to 7-membered heterocycloalkyl) C_0 - C_4 alkyl, phenyl C_0 - C_6 alkyl, pyridyl C_0 - C_6 alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl, such that if L is a single bond, then R_5 and R_6 are not phenyl or pyridyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is substituted with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and

R₄ is hydrogen, C₁-C₆alkyl or taken together with R_{1a} to form a fused carbocyclic ring.

44. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein R₁ represents 0 substituents.

45. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein R_{1a} is halogen, cyano, -COOH, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkylsulfonyl, or mono- and di-(C₁-C₆alkyl)sulfonamido.

46. A compound or pharmaceutically acceptable form thereof according to claim 45, wherein R_{1a} is fluoro, chloro, cyano, methyl, trifluoromethyl or methylsulfonyl.

47. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein R_{2a} represents 0 or 1 substituents.

48. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein R₂ is chosen from amino, halogen, cyano, hydroxy, C₁-C₄alkyl, C₁-C₄haloalkyl, C₁-C₄alkoxy, C₁-C₄alkylsulfonyl and mono- and di-(C₁-C₄alkyl)sulfonamido.

49. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein X is N.

50. A compound or pharmaceutically acceptable form thereof according to claim 49, wherein Y is N.

51. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein R₃ is selected from:

(i) hydrogen, halogen and C₁-C₆haloalkyl;

(ii) C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, phenyl C_0 - C_4 alkyl and pyridyl C_0 - C_4 alkyl; and
 (iii) groups of the formula $-N(R_5)(R_6)$ or $-O-R_7$, wherein:

R_5 and R_6 are:

- (a) independently chosen from hydrogen, C_1 - C_8 alkyl, C_3 - C_8 cycloalkyl, C_1 - C_8 alkenyl, C_2 - C_8 alkanoyl, benzyl and $-CH_2$ -pyridyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R_7 is hydrogen, C_1 - C_8 alkyl, C_3 - C_8 cycloalkyl(C_0 - C_4 alkyl), C_1 - C_8 alkenyl or C_2 - C_8 alkanoyl;

wherein each of (ii) and (iii) is substituted on from 0 to 3 carbon atoms with substituents independently chosen from halogen, cyano, amino, hydroxy, C_1 - C_6 alkyl, C_3 - C_8 cycloalkyl, C_2 - C_6 alkyl ether, C_1 - C_6 alkoxy, C_2 - C_6 alkanoyl, C_1 - C_6 haloalkyl, mono- and di-(C_1 - C_6 alkyl)amino and 4- to 8-membered heterocycloalkyl.

52. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein R_3 is:

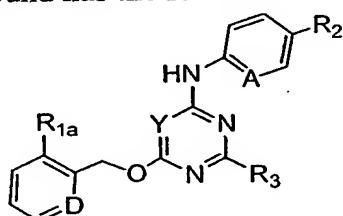
- (i) hydrogen, halogen, hydroxy or amino; or
- (ii) mono- or di-(C_1 - C_6 alkyl)amino, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl, benzyloxy, benzylamino, O - CH_2 -pyridyl or $-N$ - CH_2 -pyridyl, each of which is substituted with from 0 to 2 substituents independently chosen from halogen, amino, hydroxy, C_1 - C_4 alkyl, cyano, C_1 - C_4 alkoxy, C_1 - C_4 haloalkyl and mono- and di-(C_1 - C_6 alkyl)amino.

53. A compound or pharmaceutically acceptable form thereof according to claim 52, wherein:

R_{1a} and R_2 are independently chosen from halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 alkylsulfonyl, or mono- and di-(C_1 - C_6 alkyl)sulfonamido; and

X is N.

54. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein the compound has the formula:



55. A compound or pharmaceutically acceptable form thereof according to claim 54, wherein:

R_{1a} and R_2 are independently chosen from halogen, cyano, C_1 - C_4 alkyl, C_1 - C_4 haloalkyl, C_1 - C_4 alkylsulfonyl, or mono- and di-(C_1 - C_6 alkyl)sulfonamido;

Y is CH or N; and

R_3 is: (i) hydrogen, halogen, hydroxy or amino; or

(ii) mono- or di-(C_1 - C_6 alkyl)amino, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl, benzyloxy, benzylamino, O - CH_2 -pyridyl or $-N$ - CH_2 -pyridyl, each of which is substituted with from 0 to 2 substituents independently chosen from halogen, amino, hydroxy, C_1 - C_4 alkyl, cyano, C_1 - C_4 alkoxy, C_1 - C_4 haloalkyl and mono- and di-(C_1 - C_6 alkyl)amino.

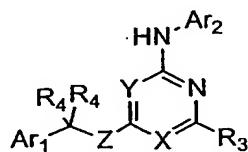
56. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein the compound exhibits no detectable agonist activity an *in vitro* assay of capsaicin receptor agonism.

57. A compound or pharmaceutically acceptable form thereof according to any one of claims 1, 28 or 43, wherein the compound has an IC_{50} value of 1 micromolar or less in a capsaicin receptor calcium mobilization assay.

58. A pharmaceutical composition, comprising at least one compound or pharmaceutically acceptable form thereof according to any one of claims 1, 28 or 43 in combination with a physiologically acceptable carrier or excipient.

59. A pharmaceutical composition according to claim 58 wherein the composition is formulated as an injectible fluid, an aerosol, a cream, a gel, a pill, a capsule, a syrup or a transdermal patch.

60. A method for reducing calcium conductance of a cellular capsaicin receptor, comprising contacting a cell expressing a capsaicin receptor with at least one compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar_1 is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R_1 ;

Ar_2 is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R_2 ;

X and Y are independently CR_x or N ; wherein R_x is independently chosen at each occurrence from hydrogen, $\text{C}_1\text{-C}_6\text{alkyl}$, amino, mono- and di-($\text{C}_1\text{-C}_6\text{alkyl}$)amino, and cyano;

Z is O or NR_z ; wherein R_z is hydrogen, $\text{C}_1\text{-C}_6\text{alkyl}$ or taken together with a R_1 moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{alkoxy}$ and $\text{C}_1\text{-C}_6\text{haloalkyl}$;

Each R_1 is independently:

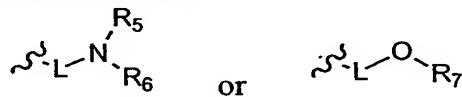
- (i) chosen from halogen, hydroxy, amino, cyano, -COOH, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{alkoxy}$, $\text{C}_2\text{-C}_6\text{alkyl}$ ether, $\text{C}_2\text{-C}_6\text{alkanoyl}$, $\text{C}_3\text{-C}_6\text{alkanone}$, $\text{C}_1\text{-C}_6\text{haloalkyl}$, $\text{C}_1\text{-C}_6\text{haloalkoxy}$, mono- and di-($\text{C}_1\text{-C}_6\text{alkyl}$)amino, $\text{C}_1\text{-C}_6\text{alkylsulfonyl}$, mono- and di-($\text{C}_1\text{-C}_6\text{alkyl}$)sulfonamido, and mono- and di-($\text{C}_1\text{-C}_6\text{alkyl}$)aminocarbonyl;
- (ii) taken together with R_z to form a fused heterocyclic ring; or
- (iii) taken together with R_4 to form a fused carbocyclic ring;

Each R_2 is independently:

- (i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{haloalkyl}$, $\text{C}_1\text{-C}_6\text{alkoxy}$, $\text{C}_1\text{-C}_6\text{haloalkoxy}$, $\text{C}_2\text{-C}_6\text{alkyl}$ ether, $\text{C}_2\text{-C}_6\text{alkanoyl}$, $\text{C}_3\text{-C}_6\text{alkanone}$, mono- and di-($\text{C}_1\text{-C}_6\text{alkyl}$)amino, $\text{C}_1\text{-C}_6\text{alkylsulfonyl}$, mono- and di-($\text{C}_1\text{-C}_6\text{alkyl}$)sulfonamido, and mono- and di-($\text{C}_1\text{-C}_6\text{alkyl}$)aminocarbonyl; or
- (ii) taken together with an adjacent R_2 to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and $\text{C}_1\text{-C}_6\text{alkyl}$;

R_3 is selected from:

- (i) hydrogen, hydroxy and halogen;
- (ii) $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{C}_3\text{-C}_8\text{cycloalkyl}$, phenyl $\text{C}_0\text{-C}_4\text{alkyl}$ and pyridyl $\text{C}_0\text{-C}_4\text{alkyl}$; and
- (iii) groups of the formula



wherein

L is a single covalent bond or $\text{C}_1\text{-C}_6\text{alkylene}$;

R_5 and R_6 are:

- (a) independently chosen from hydrogen, $\text{C}_1\text{-C}_8\text{alkyl}$, $\text{C}_1\text{-C}_8\text{alkenyl}$, $\text{C}_2\text{-C}_8\text{alkanoyl}$, ($\text{C}_3\text{-C}_8\text{cycloalkyl}$) $\text{C}_0\text{-C}_4\text{alkyl}$, (3- to 7-membered heterocycloalkyl) $\text{C}_0\text{-C}_4\text{alkyl}$, phenyl $\text{C}_0\text{-C}_6\text{alkyl}$, pyridyl $\text{C}_0\text{-C}_6\text{alkyl}$ and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or

(b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and
each R₄ is hydrogen, C₁-C₆alkyl or taken together with a R₁ to form a fused carbocyclic ring; and thereby reducing calcium conductance of the capsaicin receptor.

61. A method according to claim 60, wherein the cell is contacted *in vivo* in an animal.

62. A method according to claim 61, wherein the cell is a neuronal cell.

63. A method according to claim 60, wherein the cell is a urothelial cell.

64. A method according to claim 61, wherein during contact the compound or pharmaceutically acceptable form thereof is present within a body fluid of the animal.

65. A method according to claim 61, wherein the compound or pharmaceutically acceptable form thereof is present in the blood of the animal at a concentration of 1 micromolar or less.

66. A method according to claim 65, wherein the compound is present in the blood of the animal at a concentration of 500 nanomolar or less.

67. A method according to claim 66, wherein the compound is present in the blood of the animal at a concentration of 100 nanomolar or less.

68. A method according to claim 61, wherein the animal is a human.

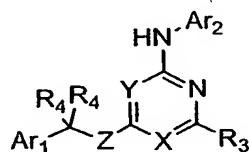
69. A method according to claim 61, wherein the compound or pharmaceutically acceptable form thereof is administered orally.

70. A method according to claim 60, wherein the compound is a compound according to claim 1.

71. A method according to claim 60, wherein the compound is a compound according to claim 28.

72. A method according to claim 60, wherein the compound is a compound according to claim 43.

73. A method for inhibiting binding of vanilloid ligand to a capsaicin receptor *in vitro*, the method comprising contacting capsaicin receptor with at least one compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar_1 is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R_1 ;

Ar_2 is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R_2 ;

X and Y are independently CR_x or N ; wherein R_x is independently chosen at each occurrence from hydrogen, $\text{C}_1\text{-C}_6$ alkyl, amino, mono- and di-($\text{C}_1\text{-C}_6$ alkyl)amino, and cyano;

Z is O or NR_z ; wherein R_z is hydrogen, $\text{C}_1\text{-C}_6$ alkyl or taken together with a R_1 moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy and $\text{C}_1\text{-C}_6$ haloalkyl;

Each R_1 is independently:

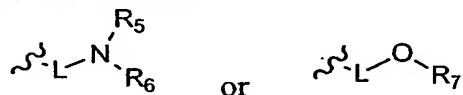
- (i) chosen from halogen, hydroxy, amino, cyano, -COOH, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, $\text{C}_2\text{-C}_6$ alkyl ether, $\text{C}_2\text{-C}_6$ alkanoyl, $\text{C}_3\text{-C}_6$ alkanone, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_1\text{-C}_6$ haloalkoxy, mono- and di-($\text{C}_1\text{-C}_6$ alkyl)amino, $\text{C}_1\text{-C}_6$ alkylsulfonyl, mono- and di-($\text{C}_1\text{-C}_6$ alkyl)sulfonamido, and mono- and di-($\text{C}_1\text{-C}_6$ alkyl)aminocarbonyl;
- (ii) taken together with R_z to form a fused heterocyclic ring; or
- (iii) taken together with R_4 to form a fused carbocyclic ring;

Each R₂ is independently:

- (i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or
- (ii) taken together with an adjacent R₂ to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and C₁-C₆alkyl;

R₃ is selected from:

- (i) hydrogen, hydroxy and halogen;
- (ii) C₁-C₆alkyl, C₃-C₈cycloalkyl, phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and
- (iii) groups of the formula



wherein

L is a single covalent bond or C₁-C₆alkylene;

R₅ and R₆ are:

- (a) independently chosen from hydrogen, C₁-C₈alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 7-membered heterocycloalkyl)C₀-C₄alkyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and

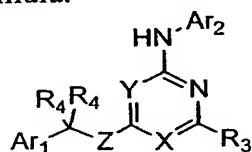
each R₄ is hydrogen, C₁-C₆alkyl or taken together with a R₁ to form a fused carbocyclic ring; under conditions and in an amount sufficient to detectably inhibit vanilloid ligand binding to capsaicin receptor.

74. A method according to claim 73, wherein the compound is a compound according to claim 1.

75. A method according to claim 73, wherein the compound is a compound according to claim 28.

76. A method according to claim 73, wherein the compound is a compound according to claim 43.

77. A method for inhibiting binding of vanilloid ligand to a capsaicin receptor in a patient, the method comprising contacting cells expressing capsaicin receptor with at least one compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar₁ is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R₁;

Ar₂ is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R₂;

X and Y are independently CR_x or N; wherein R_x is independently chosen at each occurrence from hydrogen, C₁-C₆alkyl, amino, mono- and di-(C₁-C₆alkyl)amino, and cyano;

Z is O or NR_z; wherein R_z is hydrogen, C₁-C₆alkyl or taken together with a R₁ moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C₁-C₆alkyl, C₁-C₆alkoxy and C₁-C₆haloalkyl;

Each R₁ is independently:

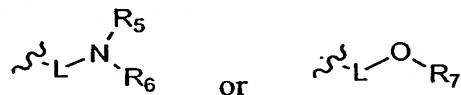
- (i) chosen from halogen, hydroxy, amino, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;
- (ii) taken together with R_z to form a fused heterocyclic ring; or
- (iii) taken together with R₄ to form a fused carbocyclic ring;

Each R₂ is independently:

- (i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or
- (ii) taken together with an adjacent R₂ to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and C₁-C₆alkyl;

R₃ is selected from:

- (i) hydrogen, hydroxy and halogen;
- (ii) C₁-C₆alkyl, C₃-C₈cycloalkyl, phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and
- (iii) groups of the formula



wherein

L is a single covalent bond or C₁-C₆alkylene;

R₅ and R₆ are:

- (a) independently chosen from hydrogen, C₁-C₈alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 7-membered heterocycloalkyl)C₀-C₄alkyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and

each R₄ is hydrogen, C₁-C₆alkyl or taken together with a R₁ to form a fused carbocyclic ring; in an amount sufficient to detectably inhibit vanilloid ligand binding to cells expressing a cloned capsaicin receptor *in vitro*, and thereby inhibiting binding of vanilloid ligand to the capsaicin receptor in the patient.

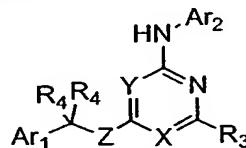
78. A method according to claim 77, wherein the compound or pharmaceutically acceptable form thereof is present in the blood of the patient at a concentration of 1 micromolar or less.

79. A method according to claim 77, wherein the compound is a compound according to claim 1.

80. A method according to claim 77, wherein the compound is a compound according to claim 28.

81. A method according to claim 77, wherein the compound is a compound according to claim 43.

82. A method for treating a condition responsive to capsaicin receptor modulation in a patient, comprising administering to the patient a capsaicin receptor modulatory amount of a compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar₁ is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R₁;

Ar₂ is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R₂;

X and Y are independently CR_x or N; wherein R_x is independently chosen at each occurrence from hydrogen, C₁-C₆alkyl, amino, mono- and di-(C₁-C₆alkyl)amino, and cyano;

Z is O or NR_z; wherein R_z is hydrogen, C₁-C₆alkyl or taken together with a R₁ moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C₁-C₆alkyl, C₁-C₆alkoxy and C₁-C₆haloalkyl;

Each R₁ is independently:

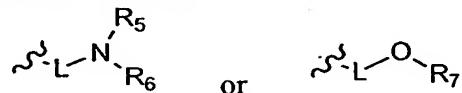
- (i) chosen from halogen, hydroxy, amino, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;
- (ii) taken together with R_z to form a fused heterocyclic ring; or
- (iii) taken together with R₄ to form a fused carbocyclic ring;

Each R₂ is independently:

- (i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or
- (ii) taken together with an adjacent R₂ to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and C₁-C₆alkyl;

R₃ is selected from:

- (i) hydrogen, hydroxy and halogen;
- (ii) C₁-C₆alkyl, C₃-C₈cycloalkyl, phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and
- (iii) groups of the formula



wherein

L is a single covalent bond or C₁-C₆alkylene;

R₅ and R₆ are:

- (a) independently chosen from hydrogen, C₁-C₈alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 7-membered heterocycloalkyl)C₀-C₄alkyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and

each R₄ is hydrogen, C₁-C₆alkyl or taken together with a R₁ to form a fused carbocyclic ring; and thereby alleviating the condition in the patient.

83. A method according to claim 82, wherein the patient is suffering from (i) exposure to capsaicin, (ii) burn or irritation due to exposure to heat, (iii) burns or irritation due to exposure to light, (iv) burn, bronchoconstriction or irritation due to exposure to tear gas, air pollutants or pepper spray, or (v) burn or irritation due to exposure to acid.

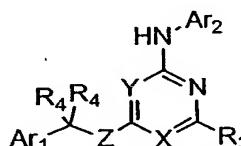
84. A method according to claim 82, wherein the condition is asthma or chronic obstructive pulmonary disease.

85. A method according to claim 82, wherein the compound is a compound according to claim 1.

86. A method according to claim 82, wherein the compound is a compound according to claim 28.

87. A method according to claim 82, wherein the compound is a compound according to claim 43.

88. A method for treating pain in a patient, comprising administering to a patient suffering from pain a capsaicin receptor modulatory amount of at least one compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar₁ is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R₁;

Ar₂ is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R₂;

X and Y are independently CR_x or N; wherein R_x is independently chosen at each occurrence from hydrogen, C₁-C₆alkyl, amino, mono- and di-(C₁-C₆alkyl)amino, and cyano;

Z is O or NR_z; wherein R_z is hydrogen, C₁-C₆alkyl or taken together with a R₁ moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C₁-C₆alkyl, C₁-C₆alkoxy and C₁-C₆haloalkyl;

Each R₁ is independently:

(i) chosen from halogen, hydroxy, amino, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;

(ii) taken together with R_z to form a fused heterocyclic ring; or

(iii) taken together with R₄ to form a fused carbocyclic ring;

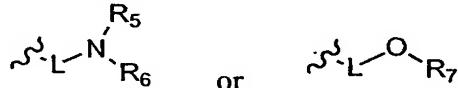
Each R₂ is independently:

(i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or

(ii) taken together with an adjacent R₂ to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and C₁-C₆alkyl;

R₃ is selected from:

- (i) hydrogen, hydroxy and halogen;
- (ii) C₁-C₆alkyl, C₃-C₈cycloalkyl, phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and
- (iii) groups of the formula



wherein

L is a single covalent bond or C₁-C₆alkylene;

R₅ and R₆ are:

- (a) independently chosen from hydrogen, C₁-C₈alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 7-membered heterocycloalkyl)C₀-C₄alkyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and

each R₄ is hydrogen, C₁-C₆alkyl or taken together with a R₁ to form a fused carbocyclic ring; and thereby alleviating pain in the patient.

89. A method according to claim 88, wherein the compound is present in the blood of the patient at a concentration of 1 micromolar or less.

90. A method according to claim 89, wherein the compound is present in the blood of the patient at a concentration of 500 nanomolar or less.

91. A method according to claim 89, wherein the compound is present in the blood of the patient at a concentration of 100 nanomolar or less.

92. A method according to claim 88, wherein the patient is suffering from neuropathic pain.

93. A method according to claim 88, wherein the pain is associated with a condition selected from: postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, toothache, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, neuritis, neuronitis, neuralgia, AIDS-related neuropathy, MS-related neuropathy, spinal cord injury-related pain, surgery-related pain, musculoskeletal pain, back pain, headache, migraine, angina, labor, hemorrhoids, dyspepsia, Charcot's pains, intestinal gas, menstruation, cancer, venom exposure, irritable bowel syndrome, inflammatory bowel disease and trauma.

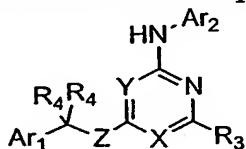
94. A method according to claim 88, wherein the patient is a human.

95. A method according to claim 88, wherein the compound is a compound according to claim 1.

96. A method according to claim 88, wherein the compound is a compound according to claim 28.

97. A method according to claim 88, wherein the compound is a compound according to claim 43.

98. A method for treating itch in a patient, comprising administering to a patient a capsaicin receptor modulatory amount of a compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar_1 is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R_1 ;

Ar_2 is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R_2 ;

X and Y are independently CR_x or N; wherein R_x is independently chosen at each occurrence from hydrogen, $\text{C}_1\text{-C}_6$ alkyl, amino, mono- and di-($\text{C}_1\text{-C}_6$ alkyl)amino, and cyano;

Z is O or NR_z ; wherein R_z is hydrogen, $\text{C}_1\text{-C}_6$ alkyl or taken together with a R_1 moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy and $\text{C}_1\text{-C}_6$ haloalkyl;

Each R_1 is independently:

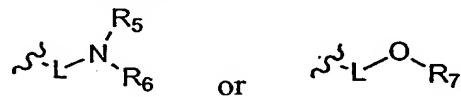
- (i) chosen from halogen, hydroxy, amino, cyano, -COOH, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ alkoxy, $\text{C}_2\text{-C}_6$ alkyl ether, $\text{C}_2\text{-C}_6$ alkanoyl, $\text{C}_3\text{-C}_6$ alkanone, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_1\text{-C}_6$ haloalkoxy, mono- and di-($\text{C}_1\text{-C}_6$ alkyl)amino, $\text{C}_1\text{-C}_6$ alkylsulfonyl, mono- and di-($\text{C}_1\text{-C}_6$ alkyl)sulfonamido, and mono- and di-($\text{C}_1\text{-C}_6$ alkyl)aminocarbonyl;
- (ii) taken together with R_2 to form a fused heterocyclic ring; or
- (iii) taken together with R_4 to form a fused carbocyclic ring;

Each R_2 is independently:

- (i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_1\text{-C}_6$ haloalkyl, $\text{C}_1\text{-C}_6$ alkoxy, $\text{C}_1\text{-C}_6$ haloalkoxy, $\text{C}_2\text{-C}_6$ alkyl ether, $\text{C}_2\text{-C}_6$ alkanoyl, $\text{C}_3\text{-C}_6$ alkanone, mono- and di-($\text{C}_1\text{-C}_6$ alkyl)amino, $\text{C}_1\text{-C}_6$ alkylsulfonyl, mono- and di-($\text{C}_1\text{-C}_6$ alkyl)sulfonamido, and mono- and di-($\text{C}_1\text{-C}_6$ alkyl)aminocarbonyl; or
- (ii) taken together with an adjacent R_2 to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and $\text{C}_1\text{-C}_6$ alkyl;

R_3 is selected from:

- (i) hydrogen, hydroxy and halogen;
- (ii) $\text{C}_1\text{-C}_6$ alkyl, $\text{C}_3\text{-C}_8$ cycloalkyl, phenyl $\text{C}_0\text{-C}_4$ alkyl and pyridyl $\text{C}_0\text{-C}_4$ alkyl; and
- (iii) groups of the formula



wherein

L is a single covalent bond or $\text{C}_1\text{-C}_6$ alkylene;

R_5 and R_6 are:

- (a) independently chosen from hydrogen, $\text{C}_1\text{-C}_8$ alkyl, $\text{C}_1\text{-C}_8$ alkenyl, $\text{C}_2\text{-C}_8$ alkanoyl, ($\text{C}_3\text{-C}_8$ cycloalkyl) $\text{C}_0\text{-C}_4$ alkyl, (3- to 7-membered heterocycloalkyl) $\text{C}_0\text{-C}_4$

C_4 alkyl, phenyl C_0-C_6 alkyl, pyridyl C_0-C_6 alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or

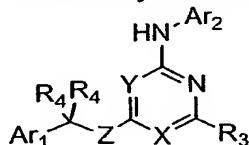
(b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R_7 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl(C_0-C_4 alkyl), C_1-C_8 alkenyl, C_2-C_8 alkanoyl, phenyl C_0-C_6 alkyl, pyridyl C_0-C_6 alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, C_2-C_6 alkyl ether, C_1-C_6 alkoxy, C_2-C_6 alkanoyl, C_1-C_6 haloalkyl, mono- and di-(C_1-C_6 alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C_1-C_4 alkyl, C_1-C_4 alkoxy and C_1-C_4 haloalkyl; and

each R_4 is hydrogen, C_1-C_6 alkyl or taken together with a R_1 to form a fused carbocyclic ring; and thereby alleviating itch in the patient.

99. A method for treating cough or hiccup in a patient, comprising administering to a patient a capsaicin receptor modulatory amount of a compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar_1 is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R_1 ;

Ar_2 is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R_2 ;

X and Y are independently CR_x or N; wherein R_x is independently chosen at each occurrence from hydrogen, C_1-C_6 alkyl, amino, mono- and di-(C_1-C_6 alkyl)amino, and cyano;

Z is O or NR_z ; wherein R_z is hydrogen, C_1-C_6 alkyl or taken together with a R_1 moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C_1-C_6 alkyl, C_1-C_6 alkoxy and C_1-C_6 haloalkyl;

Each R_1 is independently:

- (i) chosen from halogen, hydroxy, amino, cyano, -COOH, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkyl ether, C_2-C_6 alkanoyl, C_3-C_6 alkanone, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, mono- and di-(C_1-C_6 alkyl)amino, C_1-C_6 alkylsulfonyl, mono- and di-(C_1-C_6 alkyl)sulfonamido, and mono- and di-(C_1-C_6 alkyl)aminocarbonyl;

(ii) taken together with R_z to form a fused heterocyclic ring; or

(iii) taken together with R₄ to form a fused carbocyclic ring;

Each R₂ is independently:

(i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or

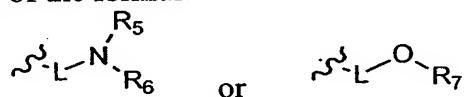
(ii) taken together with an adjacent R₂ to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and C₁-C₆alkyl;

R₃ is selected from:

(i) hydrogen, hydroxy and halogen;

(ii) C₁-C₆alkyl, C₃-C₈cycloalkyl, phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and

(iii) groups of the formula



wherein

L is a single covalent bond or C₁-C₆alkylene;

R₅ and R₆ are:

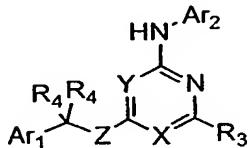
- (a) independently chosen from hydrogen, C₁-C₈alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 7-membered heterocycloalkyl)C₀-C₄alkyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or
- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and

each R₄ is hydrogen, C₁-C₆alkyl or taken together with a R₁ to form a fused carbocyclic ring; and thereby alleviating cough or hiccup in the patient.

100. A method for treating urinary incontinence or overactive bladder in a patient, comprising administering to a patient a capsaicin receptor modulatory amount of a compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar₁ is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R₁;

Ar₂ is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R₂;

X and Y are independently CR_x or N; wherein R_x is independently chosen at each occurrence from hydrogen, C₁-C₆alkyl, amino, mono- and di-(C₁-C₆alkyl)amino, and cyano;

Z is O or NR_z; wherein R_z is hydrogen, C₁-C₆alkyl or taken together with a R₁ moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C₁-C₆alkyl, C₁-C₆alkoxy and C₁-C₆haloalkyl;

Each R₁ is independently:

(i) chosen from halogen, hydroxy, amino, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;

(ii) taken together with R_z to form a fused heterocyclic ring; or

(iii) taken together with R₄ to form a fused carbocyclic ring;

Each R₂ is independently:

(i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or

(ii) taken together with an adjacent R₂ to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and C₁-C₆alkyl;

R₃ is selected from:

- (i) hydrogen, hydroxy and halogen;
- (ii) C₁-C₆alkyl, C₃-C₈cycloalkyl, phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and
- (iii) groups of the formula



wherein

L is a single covalent bond or C₁-C₆alkylene;

R₅ and R₆ are:

(a) independently chosen from hydrogen, C₁-C₈alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 7-membered heterocycloalkyl)C₀-C₄alkyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or

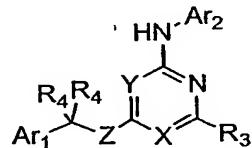
(b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and

each R₄ is hydrogen, C₁-C₆alkyl or taken together with a R₁ to form a fused carbocyclic ring; and thereby alleviating urinary incontinence or overactive bladder in the patient.

101. A method for promoting weight loss in an obese patient, comprising administering to a patient a capsaicin receptor modulatory amount of a compound having the formula:



or a pharmaceutically acceptable form thereof, wherein:

Ar₁ is phenyl or a 6-membered aromatic heterocycle, each of which is substituted with from 0 to 4 substituents independently chosen from R₁;

Ar₂ is phenyl, pyridyl or pyrimidyl, each of which is substituted with from 0 to 4 substituents independently chosen from R₂;

X and Y are independently CR_x or N; wherein R_x is independently chosen at each occurrence from hydrogen, C₁-C₆alkyl, amino, mono- and di-(C₁-C₆alkyl)amino, and cyano;

Z is O or NR_z; wherein R_z is hydrogen, C₁-C₆alkyl or taken together with a R₁ moiety to form a fused, partially saturated heterocyclic ring having from 5 to 7 ring members, wherein the fused heterocyclic ring is substituted with from 0 to 2 substituents independently chosen from halogen, cyano, C₁-C₆alkyl, C₁-C₆alkoxy and C₁-C₆haloalkyl;

Each R₁ is independently:

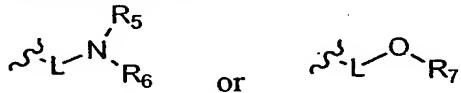
- (i) chosen from halogen, hydroxy, amino, cyano, -COOH, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, C₁-C₆haloalkyl, C₁-C₆haloalkoxy, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl;
- (ii) taken together with R_z to form a fused heterocyclic ring; or
- (iii) taken together with R₄ to form a fused carbocyclic ring;

Each R₂ is independently:

- (i) chosen from hydrogen, hydroxy, amino, cyano, halogen, -COOH, aminocarbonyl, C₁-C₆alkyl, C₁-C₆haloalkyl, C₁-C₆alkoxy, C₁-C₆haloalkoxy, C₂-C₆alkyl ether, C₂-C₆alkanoyl, C₃-C₆alkanone, mono- and di-(C₁-C₆alkyl)amino, C₁-C₆alkylsulfonyl, mono- and di-(C₁-C₆alkyl)sulfonamido, and mono- and di-(C₁-C₆alkyl)aminocarbonyl; or
- (ii) taken together with an adjacent R₂ to form a fused 5- to 10-membered carbocyclic or heterocyclic group that is substituted with from 0 to 3 substituents independently chosen from halogen and C₁-C₆alkyl;

R₃ is selected from:

- (i) hydrogen, hydroxy and halogen;
- (ii) C₁-C₆alkyl, C₃-C₈cycloalkyl, phenylC₀-C₄alkyl and pyridylC₀-C₄alkyl; and
- (iii) groups of the formula



wherein

L is a single covalent bond or C₁-C₆alkylene;

R₅ and R₆ are:

- (a) independently chosen from hydrogen, C₁-C₈alkyl, C₁-C₈alkenyl, C₂-C₈alkanoyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 7-membered heterocycloalkyl)C₀-C₄alkyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl and groups that are joined to L to form a 4- to 7-membered heterocycloalkyl; or

- (b) taken together, with the N to which they are bound, to form a 4- to 7-membered heterocycloalkyl; and

R₇ is C₁-C₈alkyl, C₃-C₈cycloalkyl(C₀-C₄alkyl), C₁-C₈alkenyl, C₂-C₈alkanoyl, phenylC₀-C₆alkyl, pyridylC₀-C₆alkyl or a group that is joined to L to form a 4- to 7-membered heterocycloalkyl;

wherein each of (ii) and (iii) is optionally substituted, preferably with from 0 to 4 substituents independently chosen from halogen, cyano, amino, hydroxy, oxo, C₁-C₆alkyl, C₃-C₈cycloalkyl, C₂-C₆alkyl ether, C₁-C₆alkoxy, C₂-C₆alkanoyl, C₁-C₆haloalkyl, mono- and di-(C₁-C₆alkyl)amino, phenyl, 5- to 6-membered heteroaryl and 4- to 8-membered heterocycloalkyl, wherein each phenyl, heteroaryl and heterocycloalkyl is substituted with from 0 to 2 secondary substituents independently chosen from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₄haloalkyl; and each R₄ is hydrogen, C₁-C₆alkyl or taken together with a R₁ to form a fused carbocyclic ring; and thereby promoting weight loss in the patient.

102. A compound or pharmaceutically acceptable form thereof according to claim 1, wherein the compound or pharmaceutically acceptable form thereof is radiolabeled.

103. A compound or pharmaceutically acceptable form thereof according to claim 28, wherein the compound or pharmaceutically acceptable form thereof is radiolabeled.

104. A compound or pharmaceutically acceptable form thereof according to claim 43, wherein the compound or pharmaceutically acceptable form thereof is radiolabeled.

105. A method for determining the presence or absence of capsaicin receptor in a sample, comprising the steps of:

- (a) contacting a sample with a compound or pharmaceutically acceptable form thereof according to any one of claims 1, 28 or 43, under conditions that permit binding of the compound to capsaicin receptor; and
- (b) detecting a level of the compound bound to capsaicin receptor, and therefrom determining the presence or absence of capsaicin receptor in the sample.

106. A method according to claim 105, wherein the compound radiolabeled, and wherein the step of detection comprises the steps of:

- (i) separating unbound compound from bound compound; and
- (ii) detecting the presence or absence of bound compound in the sample.

107. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 58 in a container; and
- (b) instructions for using the composition to treat pain.

108. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 58 in a container; and
- (b) instructions for using the composition to treat cough or hiccup.

109. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 58 in a container; and
- (b) instructions for using the composition to treat urinary incontinence or overactive bladder.

110. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 58 in a container; and
- (b) instructions for using the composition to treat obesity.

111. The use of a compound or form thereof according to any one of claims 1-56 for the manufacture of a medicament for the treatment of a condition responsive to capsaicin receptor modulation.

112. A use according to claim 111, wherein the condition is pain, asthma, chronic obstructive pulmonary disease, cough, hiccup, obesity, urinary incontinence or overactive bladder, exposure to capsaicin, burn or irritation due to exposure to heat, burn or irritation due to exposure to light, burn, bronchoconstriction or irritation due to exposure to tear gas, air pollutants or pepper spray, or burn or irritation due to exposure to acid.

113. (*4-tert-Butyl-phenyl*)-[4-(4-methyl-piperazin-1-yl)-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]-amine or a pharmaceutically acceptable form thereof.

114. (*4-tert-Butyl-phenyl*)-[4-chloro-6-(2-chloro-benzyloxy)-[1,3,5]triazin-2-yl]-amine or a pharmaceutically acceptable form thereof.

115. (*4-tert-Butyl-phenyl*)-[4-chloro-6-(2-methoxy-benzyloxy)-[1,3,5]triazin-2-yl]-amine or a pharmaceutically acceptable form thereof.

116. (*4-tert-Butyl-phenyl*)-[4-chloro-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]-amine or a pharmaceutically acceptable form thereof.

117. (*4-tert-Butyl-phenyl*)-[4-chloro-6-(3,4-dihydro-1*H*-isoquinolin-2-yl)-[1,3,5]triazin-2-yl]-amine or a pharmaceutically acceptable form thereof.

118. (*4-tert-Butyl-phenyl*)-[4-chloro-6-(6,7-dimethoxy-3,4-dihydro-1*H*-isoquinolin-2-yl)-[1,3,5]triazin-2-yl]-amine or a pharmaceutically acceptable form thereof.

119. (*4-tert-Butyl-phenyl*)-[4-chloro-6-(6,7-dimethoxy-3-methyl-3,4-dihydro-1*H*-isoquinolin-2-yl)-[1,3,5]triazin-2-yl]-amine or a pharmaceutically acceptable form thereof.

120. (4-*tert*-Butyl-phenyl)-[6-(2-trifluoromethyl-benzyloxy)-pyrimidin-4-yl]-amine or a pharmaceutically acceptable form thereof.

121. [4-(2-Chloro-phenyl)-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]-(4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

122. [4-(2-Trifluoromethyl-benzyloxy)-6-(2-trifluoromethyl-phenyl)-[1,3,5]triazin-2-yl]-(4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

123. [4,6-Bis-(2-chloro-benzyloxy)-[1,3,5]triazin-2-yl]-(4-*tert*-butyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

124. [4,6-Bis-(2-fluoro-benzyloxy)-[1,3,5]triazin-2-yl]-(4-*tert*-butyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

125. [4,6-Bis-(2-methoxy-benzyloxy)-[1,3,5]triazin-2-yl]-(4-*tert*-butyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

126. [4,6-Bis-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]-(4-*tert*-butyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

127. [4,6-Bis-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]-(4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

128. [4,6-Bis-(3-chloro-pyridin-2-ylmethoxy)-[1,3,5]triazin-2-yl]-(4-*tert*-butyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

129. [4,6-Bis-(pyridin-2-ylmethoxy)-[1,3,5]triazin-2-yl]-(4-*tert*-butyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

130. [4-Chloro-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]-(4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

131. [4-Cyclopentyloxy-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]-(4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

132. [4-Ethoxy-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]-(4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

133. [4-Morpholin-4-yl-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]- (4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

134. [4-Phenyl-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]- (4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

135. [4-Pyridin-3-yl-6-(2-trifluoromethyl-benzyloxy)-[1,3,5]triazin-2-yl]- (4-trifluoromethyl-phenyl)-amine or a pharmaceutically acceptable form thereof.

136. 2-Methyl-4-[4-(2-trifluoromethyl-benzyloxy)-6-(4-trifluoromethyl- phenylamino)-[1,3,5]triazin-2-ylamino]-butan-2-ol or a pharmaceutically acceptable form thereof.

137. 4-(2-Trifluoromethyl-benzyloxy)-6-(4-trifluoromethyl-phenylamino)- [1,3,5]triazin-2-ol or a pharmaceutically acceptable form thereof.

138. 6-Methyl-N-(2-trifluoromethyl-benzyl)-N'-(4-trifluoromethyl-phenyl)- [1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

139. N-(2-Methoxy-ethyl)-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl- phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

140. N-(2-Morpholin-4-yl-ethyl)-6-(2-trifluoromethyl-benzyloxy)-N'-(4- trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

141. N-(3-Methyl-butyl)-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl- phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

142. N-(4-*tert*-Butyl-phenyl)-6-(2-chloro-benzyloxy)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

143. N-(4-*tert*-Butyl-phenyl)-6-(2-fluoro-benzyloxy)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

144. N-(4-*tert*-Butyl-phenyl)-6-(2-methoxy-benzyloxy)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

145. N-(4-*tert*-Butyl-phenyl)-6-chloro-N'-(2-chloro-benzyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

146. N-(4-*tert*-Butyl-phenyl)-6-chloro-N'-(2-fluoro-benzyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

147. N-(4-*tert*-Butyl-phenyl)-6-chloro-N'-(2-methoxy-benzyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

148. N-(4-*tert*-Butyl-phenyl)-6-chloro-N'-(2-trifluoromethyl-benzyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

149. N-(4-*tert*-Butyl-phenyl)-N'-(2-chloro-benzyl)-[1,3,5]triazine-2,4,6-triamine or a pharmaceutically acceptable form thereof.

150. N-(4-*tert*-Butyl-phenyl)-N'-(2-chloro-benzyl)-6-ethoxy-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

151. N-(4-*tert*-Butyl-phenyl)-N'-(2-chloro-benzyl)-6-methoxy-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

152. N-(4-*tert*-Butyl-phenyl)-N'-(2-chloro-benzyl)-6-methyl-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

153. N-(4-*tert*-Butyl-phenyl)-N'-(2-chloro-benzyl)-N"-methyl-[1,3,5]triazine-2,4,6-triamine or a pharmaceutically acceptable form thereof.

154. N-(4-*tert*-Butyl-phenyl)-N'-(2-chloro-benzyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

155. N-(4-*tert*-Butyl-phenyl)-N'-(2-fluoro-benzyl)-[1,3,5]triazine-2,4,6-triamine or a pharmaceutically acceptable form thereof.

156. N-(4-*tert*-Butyl-phenyl)-N'-(2-fluoro-benzyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

157. N-(4-*tert*-Butyl-phenyl)-N'-(2-methoxy-benzyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

158. N-(4-*tert*-Butyl-phenyl)-N'-(2-methoxy-benzyl)-[1,3,5]triazine-2,4,6-triamine or a pharmaceutically acceptable form thereof.

159. N-(4-*tert*-Butyl-phenyl)-N'-(2-methoxy-benzyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

160. N-(4-*tert*-Butyl-phenyl)-N'-(2-trifluoromethyl-benzyl)-[1,3,5]triazine-2,4,6-triamine or a pharmaceutically acceptable form thereof.

161. N-(4-*tert*-Butyl-phenyl)-N'-(2-trifluoromethyl-benzyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

162. N-(4-*tert*-Butyl-phenyl)-N'-(3-fluoro-benzyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

163. N-(4-*tert*-Butyl-phenyl)-N'-(3-methoxy-benzyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

164. N-(4-*tert*-Butyl-phenyl)-N'-(4-chloro-benzyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

165. N-(4-*tert*-Butyl-phenyl)-N'-(4-methoxy-benzyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

166. N-(4-*tert*-Butyl-phenyl)-N',N"-bis-(2-chloro-benzyl)-[1,3,5]triazine-2,4,6-triamine or a pharmaceutically acceptable form thereof.

167. N-(4-*tert*-Butyl-phenyl)-N',N"-bis-(2-methoxy-benzyl)-[1,3,5]triazine-2,4,6-triamine or a pharmaceutically acceptable form thereof.

168. N-(4-*tert*-Butyl-phenyl)-N'-pyridin-2-ylmethyl-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

169. N-(4-*tert*-Butyl-phenyl)-N'-pyridin-3-ylmethyl-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

170. N-(4-*tert*-Butyl-phenyl)-N'-pyridin-4-ylmethyl-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

171. N,N-Diethyl-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

172. N4-(4-*tert*-Butyl-phenyl)-6-(2-trifluoromethyl-benzyloxy)-pyrimidine-2,4-diamine or a pharmaceutically acceptable form thereof.

173. N-Benzyl-N'-(4-*tert*-butyl-phenyl)-pyrimidine-4,6-diamine or a pharmaceutically acceptable form thereof.

174. N-Butyl-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

175. N-Cyclobutyl-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

176. N-Cyclohexyl-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

177. N-Cyclopentyl-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

178. N-Isobutyl-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

179. N-Isopropyl-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.

180. N-*tert*-Butyl-6-(2-trifluoromethyl-benzyloxy)-N'-(4-trifluoromethyl-phenyl)-[1,3,5]triazine-2,4-diamine or a pharmaceutically acceptable form thereof.